Citation:

Knudtson MD, Klein BE, Klein R, Shankar, AA. Associations with weight loss and subsequent mortality risk. *Ann Epidemiol.* 2005; 15: 483-491.

PubMed ID: 16029840

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To measure weight loss and subsequent mortality risks over 10 years in persons ranging in age from 43 to 86 years in a large population-based study, to determine whether or not weight loss was an independent marker for mortality.

Inclusion Criteria:

Males and females aged 43 to 86 years living in the township of Beaver Dam, WI.

Exclusion Criteria:

- Persons living outside of Beaver Dam, WI township
- Persons less than age 43 years or older than age 86 years within the township
- All persons with a potentially fatal disease at baseline
- Note that the analysis was repeated, excluding person who died within two years of the baseline examination.

Description of Study Protocol:

Recruitment

Eligible participants were identified through a private census of the population of Beaver Dam, WI between September 15, 1987 and May 4, 1988.

Design

Prospective cohort study.

Blinding Used

Yes, for use of laboratory tests, blood pressure averages.

Statistical Analysis

- Significance of differences was tested controlling for age using Cochran-Mantel-Haenszel tests for categorical variables and F-tests for continuous measures
- Logistic regression was used to model multivariate relationships with weight loss
- Mortality rates were estimated using Kaplan-Meier survival methods
- Cox proportional hazard models were used for multivariate survival analysis, adjusting for potential confounders
- A variable related to mortality and weight loss, as well as any variable changing the association between weight loss and mortality was considered a confounder
- To investigate potential interactions, stratified analyses of BMI at highest weight (less than 25, 25 to 29, more than 30kg/m^2), age (less than 65, more than 65 years), pre-existing disease status, smoking status, dieting to lose weight and exercise status were examined
- Analyses were repeated excluding persons who died within two years of the baseline examination.

Data Collection Summary:

Timing of Measurements

Mortality was ascertained between the baseline examination in 1988 to 1990 and December 31, 1999.

Dependent Variables

Variable 1: Mortality by December 31, 1999. Cause of death was defined as any contributing cause listed in the death certificate, according to the International Classification of Diseases, Ninth and Tenth (for deaths after December 31, 1998) Revision, Clinical Modification Codes.

Independent Variables

Variable 1: Percent weight loss from highest weight to the baseline examination. Calculated as 100[(weight at baseline exam-highest weight)/(highest weight)]. Weight loss categorized into four categories (loss less than 5%, loss 5% to 9.9%, loss 10% to 19.9%, loss 20% or more) to minimize bias from differences between actual and self-reported weights.

Control Variables

- Age
- Body mass index (BMI) at highest weight
- Smoking status
- Dieting to lose weight
- Exercise status
- Pre-existing disease status.

Description of Actual Data Sample:

- *Initial N:* 4,926 persons
- *Attrition (final N):* 4,926 subjects participated at baseline and follow-up
- *Age:*

- Age 43 to 64 years
  - Males: 1,481
  - Females: 1,566
- Age 65 to 86 years
  - Males: 1,174,
  - Females: 1,668
- *Ethnicity:* 99% White, 1% unspecified
- *Anthropometrics:* Fairly homogenous population for BMI
- *Location:* Beaver Dam, WI.

Summary of Results:

Findings

After controlling for age, medical and lifestyle factors, both men and women had higher mortality rates over a 10-plus-year period for increasing categories of weight loss:

- Men: [Hazard ratio (HR) and 95% CI: 1.16 (1.06, 1.27), P=0.001]
- Women: [HR (95% CI): 1.23 [1.13, 1.34], P=0.001).

Other Findings

- In all men, after adjusting for age, smoking, lifestyle and other medical factors, for each increase in weight loss category the risk of death increased by 16%. The corresponding risk for increasing weight loss and mortality for women was slightly higher at 23%.
- The majority of deaths in the population had a mention of cardiovascular disease on the death certificate (N=742, 64% of all deaths). The association with increasing weight loss category and cancer mortality was not significant in men, but was for women [multivariate HR, 95% CI: 1.07 (0.91, 1.27) for men and 1.21 (1.04, 1.41) for women].
- Persons who had lost weight had higher rates of a history of cardiovascular disease and diabetes at baseline
- Persons who reported being on special diets to lose weight who lost weight were not at increased risk of dying after adjusting for age, medical and lifestyle factors. This suggests most of the realized weight loss reflects other processes (e.g., severity of disease) associated with mortality.

Author Conclusion:

- Weight loss was associated with older age, higher rates of diseases such as diabetes and lower baseline levels of blood pressure and serum total cholesterol
- After controlling for age, medical and lifestyle factors, both men and women had higher mortality rates over a 10-plus-year period for increasing categories of weight loss
- The strong association between weight loss (likely involuntary) and mortality may be a useful way of estimating overall risks to longevity in populations.

Reviewer Comments:

- *Recruitment methods were not specified*
- *Attrition was not specified other than measured mortality. Actual mortality cited is difficult*

to ascertain, because p. 484 cites N=1,199 and in Table 2 all categories for men and women add to N=1,124 deaths. It is unclear if the difference is from excluded deaths in the first two years of the study.

- *Description of actual data section: Tables 3A and B were used to calculate the number of males and females. The total does not add up to the 4,926 persons mentioned in the study. N total + N death = 5,889, and N total alone is 4,765. Total death listed in table is 1,124 and not the 1,199 cited in the narrative.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes

3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	Yes
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	Yes
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A

6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes

8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes